IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

HORIZON MEDICINES LLC, *Plaintiff*, v. ALKEM LABORATORIES LTD., *Defendant*.	)	C.A. No. 1:18-cv-01014-RGA [redacted] Public Version Filed: July 17, 2020

OPENING BRIEF IN SUPPORT OF DEFENDANT'S MOTION TO EXCLUDE EXPERT TESTIMONY OF STEVEN R. LITTLE, PH.D.

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TABLE OF CONTENTS

I. INTRODUCTION. 1

II. BACKGROUND. 1

A. The Asserted Claims of the '451 Patent. 1

B. Alkem's ANDA Product. 2

C. Dr. Little's Infringement Opinions. 2

III. LEGAL STANDARDS. 2

IV. ARGUMENT 3

A. The Court Should Exclude Dr. Little's Opinions that Alkem's ANDA Product Infringes the Barrier Layer Limitation Under DOE as He Fails to Evaluate the Asserted Claims on a Limitation-by-Limitation Basis. 3

B. Dr. Little's Analysis Fails to Consider that Horizon Dedicated Certain Components Found in Alkem's Barrier Layer. 6

C. The Court Should Exclude Dr. Little's Infringement Opinions Concerning the "Surrounds the Second Portion" Limitation of the '451 Patent Claims. 7

V. CONCLUSION. 9

TABLE OF AUTHORITIES

Federal Cases

Akzo Nobel Coatings, Inc. v. Dow Chem. Co.,
811 F.3d 1334 (Fed. Cir. 2016) 5, 8

Bicon, Inc. v. Straumann Co.,
441 F.3d 945 (Fed. Cir. 2006) 8, 9

Carnegie Mellon Univ. v. Hoffman-La Roche Inc.,
541 F.3d 1115 (Fed. Cir. 2008) 8

Cave v. Saxon Mortg. Servs. Inc.,
C.A. Nos. 11-4586, 12-5366, 2015 WL 6153754 (E.D. Pa. Oct. 20, 2015) 3

Daubert v. Merrell Dow Pharm., Inc.,
509 U.S. 579 (1993) 2, 3

Eagle Pharm., Inc. v. Slayback Pharma LLC,
958 F.3d 1171 (Fed. Cir. 2020) 7

Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp.,
149 F.3d 1309 (Fed. Cir. 1998) 9

In re Bendamustine Consol. Cases,
C.A. No. 13-2046-GMS, 2015 WL 1951399 (D. Del. Apr. 29, 2015) 7

Indivior Inc. v. Dr. Reddy's Labs., S.A.,
930 F.3d 1325 (Fed. Cir. 2019) 7

Intellectual Ventures I LLC v. Xilinx, Inc.,
C.A. No. 10-1065-LPS, 2014 WL 1814384 (D. Del. Apr. 14, 2014) 3

Izumi Prod. Co. v. Koninklijke Philips Elecs. N.V.,
315 F. Supp. 2d 589 (D. Del. 2004) 2

Izumi Prod. Co. v. Koninklijke Philips Elecs. N.V.,
140 F. App'x 236 (Fed. Cir. 2005) 2

Mylan Institutional LLC v. Aurobindo Pharma Ltd.,
857 F.3d 858 (Fed. Cir. 2017) 5

Padillas v. Stork-Gamco,
186. F.3d 412 (3d Cir. 1999) 3

Reckitt Benckiser Pharm., Inc. v. Dr. Reddy's Labs., SA,
Civil Action No. 14-1451-RGA, 2017 WL 3782782 (D. Del. Aug. 31, 2017) 6

Tex. Instruments Inc. v. Cypress Semiconductor Corp.,
90 F.3d 1558 (Fed. Cir. 1996) 8

Tronzo v. Biomet, Inc.,
156 F.3d 1154 (Fed. Cir. 1998) 9

UGI Sunbury LLC v. A Permanent Easement for 1.7575 Acres,
949 F.3d 825 (3d Cir. 2020) 3

Warner-Jenkinson Co. v. Hilton Davis Chem. Co.,
520 U.S. 17 (1997) 3

Federal Rules

FED. R. EVID. 702 ..... 1, 2

I. INTRODUCTION.

Pursuant to the governing Scheduling Order (D.I. 21, D.I. 131), Defendant Alkem Laboratories, Inc. hereby moves under Federal Rule of Evidence ("FRE") 702 to exclude infringement opinions of Horizon's proposed expert Steven R. Little, Ph.D. relating to the asserted claims of U.S. Patent No. 8,067,451 ("the '451 patent") under the doctrine of equivalents ("DOE").[1] As relevant to the '451 patent claim limitation "wherein a barrier layer comprising hydroxy[l] propyl methyl cellulose 2910, polyoxyethylene glycol 400, polysorbate 80, and titanium dioxide surrounds the second portion completely separating it from the first portion," Dr. Little does not perform a limitation-by-limitation (i.e., component-by-component) analysis; rather, his analysis is limited to analyzing the entirety of that barrier layer wherein clause as a "collection of excipients." As such, he failed to apply the correct legal standard, and the Court should exclude his DOE opinions as unreliable.

II. BACKGROUND.

A. The Asserted Claims of the '451 Patent.

The '451 patent asserted claims (1-3, 8-10) require a barrier layer specifically containing (i) hydroxy[l] propyl methyl cellulose ("HPMC") 2910; (ii) polyoxyethylene glycol ("PEG") 400; (iii) polysorbate 80; and (iv) titanium dioxide that "surrounds the second portion [famotidine] completely separating it from the first portion [ibuprofen]" (the "barrier layer limitation") (Ex. 1, the '451 patent at 49:54-60). The '451 patent specification broadly describes "well known" materials that can be used for the "barrier layer," including PVA and talc. (*Id.* at 7:4-35, 19:35-65, 21:32-36, 49:5-16). However, the asserted claims only identify the four (4) specific barrier layer components enumerated above.

[1] Alkem has concurrently submitted a separate motion seeking to exclude certain opinions of Horizon's proposed expert James M. Scheiman, M.D. pertaining to secondary considerations.

B. Alkem's ANDA Product.

It is undisputed that Alkem's ANDA product has [redacted] made up of (i) [redacted] (ii) [redacted], and (iii) [redacted] and [redacted]. (Ex. 2, Alkem's ANDA # 211890 [redacted] D.I. 68, Joint Claim Construction Br. at 11).

C. Dr. Little's Infringement Opinions.

Dr. Little acknowledges that Alkem's ANDA product does not literally infringe the "first portion," "second portion" and barrier layer limitations of the '451 patent asserted claims. Rather, his opinions on those limitations are limited to infringement under a DOE theory. In evaluating the barrier layer limitation, Dr. Little focused on a "collection of excipients," rather than on the four (4) separate ingredients explicitly identified in the claim (HPMC 2910, PEG 400, polysorbate 80, and titanium dioxide). In other words, he admittedly failed to compare each of the ingredients identified in the asserted claims to each of the ingredients that make up the relevant barrier layer in Alkem's ANDA product ([redacted]).

III. LEGAL STANDARDS.

Under FRE 702, expert testimony is admissible only if "the testimony is based on sufficient facts or data[.]" FRE 702(b); *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 589-92 (1993). Specifically, expert testimony must meet three distinct requirements in order to be admissible: (i) the expert providing the testimony must be qualified, (ii) the opinion must be reliable, and (iii) the testimony must help the trier of fact to understand the evidence or determine a fact in issue based on the expert's knowledge. FRE 702; *Izumi Prod. Co. v. Koninklijke Philips Elecs. N.V.*, 315 F. Supp. 2d 589, 600-01 (D. Del. 2004), *aff'd*, 140 F. App'x 236 (Fed. Cir. 2005). "The burden of establishing admissibility by a preponderance of the

evidence . . . is on the proponent." *Padillas v. Stork-Gamco*, 186. F.3d 412, 418 (3d Cir. 1999). The linchpin requirements of FRE 702 are the "reliability" of the testimony offered and its relevance, otherwise referred to as its "fit." *Daubert*, 509 U.S. at 589-92.[2]

IV. ARGUMENT.

A. The Court Should Exclude Dr. Little's Opinions that Alkem's ANDA Product Infringes the Barrier Layer Limitation Under DOE as He Fails to Evaluate the Asserted Claims on a Limitation-by-Limitation Basis.

In arriving at his opinion that Alkem infringes the barrier layer limitation under the DOE, Dr. Little evaluated the claimed barrier layer as a whole, or as he terms it, as a "collection of excipients." However, the law clearly requires that the DOE "must be applied to individual elements of the claims, not to the invention as a whole." *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 25 (1997) ("Consideration must be given to the purpose for which an ingredient is used in a patent, the qualities it has when combined with the other ingredients, and the function which it is intended to perform. An important factor is whether persons reasonably skilled in the art would have known of the interchangeability of an ingredient not contained in the patent with one that was." (citations omitted)). As such, Dr. Little applied the incorrect legal standard in evaluating infringement, rendering his opinions unreliable and inadmissible under *Daubert*. *See Intellectual Ventures I LLC v. Xilinx, Inc.*, C.A. No. 10-1065-LPS, 2014 WL 1814384, at *3-4 (D. Del. Apr. 14, 2014) (finding that plaintiff's expert's "understanding of the law is incorrect" and "opinion is not based on sufficient facts or data and he has not reliably applied the principles and methods to the facts of this case"); *Cave v. Saxon Mortg. Servs. Inc.*, C.A. Nos. 11-4586, 12-5366, 2015 WL 6153754, at *9 (E.D. Pa. Oct. 20, 2015).

[2] *Daubert* applies to bench trials, as here. *UGI Sunbury LLC v. A Permanent Easement for 1.7575 Acres*, 949 F.3d 825, 832-33 (3d Cir. 2020).

First, Dr. Little does not provide a limitation-by-limitation analysis; rather, he merely opines that the claimed barrier layer disclosed in the patent claims should be evaluated as a "collection of excipients," which renders the individual recited ingredients (i.e., HPMC 2910, PEG 400, polysorbate 80, and titanium) irrelevant to the DOE analysis:

> 248. As an initial matter, it is my opinion that a POSA would not interpret the first portion of this claim term, "a barrier layer comprising hydroxyl propyl methyl cellulose 2910, polyoxyethylene glycol 400, polysorbate 80, and titanium dioxide," on an element-by-element basis. Rather, in the case of this particular patent, it is my opinion that a POSA would understand this claim term as referring to a collection of excipients that function together as a single entity. My opinion is supported by the specification and prosecution history of the '451 patent, as well as by the general knowledge and understanding of a POSA.

(Ex. 3, Little Opening ¶ 248). Under his truncated analysis, Dr. Little fails to show how the components in Alkem's ANDA product barrier layer are insubstantially different from the claimed barrier layer, or that these components otherwise perform substantially the same function in substantially the same way with substantially the same result. (*Id.* ¶¶ 255-56, 260).[3] Instead, Dr. Little simply asserts the existence of a barrier layer that allegedly achieves a structural function is sufficient to satisfy the DOE standard:

> Second, the individual components of a film coating system interact with one another when combined together, such that the characteristics of a film-coating system are not attributable to individual components, but rather, ***to how the individual components function together***.

(Ex. 4, Little Reply ¶ 98 (emphasis added); *see also* Ex. 3, Little Opening ¶¶ 254-257, 271 (stating that all of these components combined are simply a "barrier layer" that is a "collection of excipients" and therefore infringe as performing the same "function" of "separating" the ibuprofen portion from the famotidine portion in the claimed oral dosage form)). Admittedly, at

[3] In the event the Court entertains any DOE testimony, Alkem reserves the right to challenge whether the function-way-result test is the proper test to apply in this case.

no point does Dr. Little provide a limitation-by-limitation analysis for each of the claimed components (HPMC 2910, PEG 400, polysorbate 80, and titanium dioxide) or explain how these limitations are found in Alkem's ANDA product. (Ex. 5, Little Rough Tr. at 228:13 – 229:3).

Whether considering DOE under an insubstantial differences or function-way-result test, the patentee is required to "establish 'equivalency on a limitation-by-limitation basis' by 'particularized testimony and linking argument.'" *Akzo Nobel Coatings, Inc. v. Dow Chem. Co.*, 811 F.3d 1334, 1342 (Fed. Cir. 2016). Thus, Dr. Little's analysis invites the Court to proceed in a manner that is legally deficient. *See Mylan Institutional LLC v. Aurobindo Pharma Ltd.*, 857 F.3d 858, 867 (Fed. Cir. 2017) (explaining that "each limitation must satisfy an equivalence test"). In *Mylan*, the Federal Circuit reversed a district court finding of infringement under the DOE, stating "[b]ut that is not considering the 'way' the oxidation works. Manganese dioxide and silver oxide may have the same *function*, but the question is whether they operate in the same *way*." *Id.* at 868. Here, Dr. Little's DOE analysis suffers the same deficiencies; he opines that the "function" (separating the ibuprofen portion from the famotidine portion) and the "way" (preventing the ibuprofen from chemically interacting) essentially operate in the same manner and are therefore "insubstantially different," which is inappropriate under binding legal precedent. *Id.* at 867-68.

Moreover, Dr. Little does not establish (or opine at all) that those of ordinary skill in the art would recognize the components in Alkem's barrier layer, i.e., [redacted], as equivalent to the claimed barrier layer ingredients, i.e., HPMC 2910, PEG 400, polysorbate 80, and titanium dioxide. The practical effect of his opinions is that the DOE could capture *any barrier layer*, without regard to its components or how they each individually function or perform. (*See* Ex. 5, Little Rough Tr. at 236:2-9).

B. Dr. Little's Analysis Fails to Consider that Horizon Dedicated Certain Components Found in Alkem's Barrier Layer.

Dr. Little's opinions rejecting application of the disclosure-dedication doctrine are similarly deficient. In responding to Alkem's position that Horizon disclosed certain components of Alkem's barrier layer (e.g., [redacted]) under that doctrine, Dr. Little admits that he did not consider the individual components of Alkem's barrier layer. Rather, he has opined that he simply confirmed that the barrier layer in Alkem's ANDA product is not identified by trade name, i.e., [redacted], in the '451 patent specification:

> 109. Dr. Chambliss opines that "Horizon cannot assert infringement under a doctrine of equivalents theory because it dedicated ingredients that make up the relevant barrier layer in Alkem's ANDA Product to the public, and, as such, cannot recapture that claim scope." (Chambliss Reb. Rpt. at ¶ 309.) In making such an opinion, Dr. Chambliss continues to consider each component of the claimed barrier layer on an element-by-element basis. However, as discussed at length in my Opening Report and above in Section IV.A.1.(a), I disagree that it is appropriate to consider the individual excipients recited in the "barrier layer" element of claim 1 of the '451 patent on an element-by-element basis. Accordingly, I disagree that it is appropriate to determine whether Horizon dedicated individual ingredients to the public.
>
> 110. Additionally, I note that the specific barrier layer used in [redacted] is not explicitly identified in the specification of the '451 patent. Thus, Dr. Chambliss cannot argue that Horizon dedicated this particular barrier layer to the public.

(Ex. 4, Little Reply ¶¶ 109-110; *see also* Ex. 5, Little Rough Tr. at 240:2-18).[4] Because Dr. Little admittedly ignores whether any of the ingredients in Alkem's barrier layer were dedicated, he failed to undertake the proper legal analysis. *See Reckitt Benckiser Pharm., Inc. v. Dr. Reddy's Labs., SA*, Civil Action No. 14-1451-RGA, 2017 WL 3782782, at *3 (D. Del. Aug. 31, 2017) ("[I]f one of ordinary skill in the art can understand the unclaimed disclosed teaching upon

[4] (*See also* Alkem's Response to Horizon's Supplemental Claim Construction Brief (D.I. 100); Alkem Letters dated June 18, 2020 and July 7, 2020 (D.I. 153, 156)).

reading the written description, the alternative matter disclosed has been dedicated to the public."), *aff'd sub nom. Indivior Inc. v. Dr. Reddy's Labs., S.A.*, 930 F.3d 1325 (Fed. Cir. 2019); *Eagle Pharm., Inc. v. Slayback Pharma LLC*, 958 F.3d 1171, 1176 (Fed. Cir. 2020) (DOE "requires only that the specification disclose the unclaimed matter 'as an alternative to the relevant claim limitation'").[5] Dr. Little's DOE opinions as to the barrier layer limitation should be excluded for this reason as well.

C. The Court Should Exclude Dr. Little's Infringement Opinions Concerning the "Surrounds the Second Portion" Limitation of the '451 Patent Claims.

The asserted claims of the '451 patent require that the claimed barrier layer ***surrounds the 26.6 mg famotidine*** (second) portion completely separating it from the 800 mg ibuprofen (first) portion. Dr. Little has acknowledged that Alkem's ANDA product does not literally infringe this claim limitation, but has purported to assert opinions of infringement of this limitation under a DOE theory. However, Dr. Little did not undertake any analysis to adequately establish legal equivalency with respect to how Alkem's barrier layer "surrounds" the famotidine portion completely separating it from the ibuprofen portion; instead, he offers little more than conclusory statements in support of his opinion here.

For instance, Dr. Little states the "claimed barrier layer ***must be placed in the dosage form*** such that it successfully separates the famotidine portion from the ibuprofen portion." (Ex. 3, Little Opening ¶ 255 (emphasis added); *see also id.* ¶¶ 256-257 (offering conclusory statements for "function-way-result" test). Dr. Little offers no rationale for his expansion that the barrier layer ***can be anywhere in the dosage form***, despite the clear language of independent claims 1 and 10 of the '451 patent requiring the barrier layer to ***surround the second portion***

[5] *See also In re Bendamustine Consol. Cases*, C.A. No. 13-2046-GMS, 2015 WL 1951399, at *2 (D. Del. Apr. 29, 2015) ("By claiming only TBA from among the listed organic solvents, the patentee effectively disclaimed the remaining solvents in the list and cannot employ the [DOE] to bring them back within the scope of the '190 and '863 patents.").

[famotidine]. Likewise, Dr. Little provides one conclusory paragraph for his insubstantial differences opinions: "such that sufficient stability is achieved in a way that is essentially the same as the claimed Opadry barrier layer." (*Id.* ¶ 264; *see also* Ex. 5, Little Reply ¶ 108). But this is not sufficient to satisfy Horizon's burden of establishing legal equivalency. *See Akzo*, 811 F.3d at 1342 ("A patentee must establish 'equivalency on a limitation-by-limitation basis' by 'particularized testimony and linking argument' as to the insubstantiality of the differences between the claimed invention and the accused device or process." (quoting *Tex. Instruments Inc. v. Cypress Semiconductor Corp.*, 90 F.3d 1558, 1566 (Fed. Cir. 1996))).

Moreover, the plain language of the claim evinces a clear intent that the barrier layer surrounds the famotidine (second) portion, not the ibuprofen (first) portion, regardless of whether infringement is asserted under a literal or DOE theory. Dr. Little's opinions also violate the principle that "claims are interpreted with an eye toward giving effect to all terms in the claim." *Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 950 (Fed. Cir. 2006). Dr. Little improperly reads the "surrounds the second portion completely separating it from the first portion" limitation out of the asserted claims of the '451 patent entirely, thereby violating the all-elements rule. *See Carnegie Mellon Univ. v. Hoffman-La Roche Inc.*, 541 F.3d 1115, 1128-29 (Fed. Cir. 2008). More specifically, the asserted claims of the '451 patent require a specific location for the barrier layer, i.e., surrounding the famotidine portion. Dr. Little's opinions that Alkem's barrier layer, which surrounds the [redacted], infringes even under a DOE theory is contrary to established precedent. "A claim that contains a detailed recitation of structure is properly accorded correspondingly limited recourse to the [DOE]." *Bicon*, 441 F.3d at 955 (citation omitted). The Federal Circuit has stated that "by defining the claim in a way that clearly excluded certain subject matter, the patent implicitly disclaimed the subject matter that was excluded and thereby

barred the patentee from asserting infringement under the [DOE]." *Id.* (citation omitted); *see also Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1160 (Fed. Cir. 1998) (to hold that a device with a hemispherical shape infringes a patent requiring that the device have a "generally conical outer surface" would "write the 'generally conical outer surface' limitation out of the claims"); *Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp.*, 149 F.3d 1309, 1317 (Fed. Cir. 1998) (subject matter is "specifically excluded" from the DOE if its inclusion is "inconsistent with the language of the claim")

Because Dr. Little's analysis improperly ignores the "surrounds the second portion" language and does not provide a legally sound limitation-by-limitation analysis, the Court should exclude these opinions related to the asserted claims of the '451 patent for this reason as well.

V. CONCLUSION.

For all of the reasons described herein, Defendant Alkem Laboratories Ltd. respectfully requests that the Court preclude Horizon from presenting certain opinions and testimony of its proposed expert Dr. Little as outlined herein.

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